

**AMENDMENTS TO THE DRAWINGS**

The attached sheet(s) of drawings include changes to Figure 10.

Attachment:     Replacement sheet  
                     Annotated sheet showing changes

### **REMARKS**

Claims 1-16 are pending. Claims 3, 6, and 7 are cancelled. Claims 1, 2, 4, 5, and 8-16 are currently amended. Applicants submit that no new matter has been added as a result of this amendment; support therefor can be found throughout the specification and original claims.

#### ***Information Disclosure Statement***

The Examiner asserts at page 3 of the Office Action that the listing of references presented at pages 21-22 of the instant specification is not a proper information disclosure statement. The references listed at those pages are not believed to be material to patentability. Thus, they have not been cited in an information disclosure statement.

#### ***Priority***

Applicants have amended the specification to include a reference to all related prior applications. Applicants previously identified the prior applications in the application transmittal papers and in the duly executed Declaration. The information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first official Filing Receipt. In view of the above, a petition under 37 CFR 1.78(a) and surcharge under 37 CFR 1.17(t) are not required.

#### ***Drawings***

In response to the Examiner's objection to Figure 10, Applicants submit herewith a corrected replacement Figure that includes the X-axis label.

#### ***Claim Objections***

The Examiner objected to claims 1, 4-5, 7, 9, and 10 for various informalities. Claim 5 has been cancelled. Applicants submit that in view of the amendments to

claims 1 and 5, the recited objections are rendered moot. Claims 4 and 10 have been appropriately amended to address each of the informalities.

The Examiner asserts at page 7 of the Office Action that the term "Kozak sequence", recited in claim 9, must be referred to by its sequence identification number to comply with 37 CFR 1.821. The instant specification states at page 4, paragraph 0081 of US 2004/0268432 that "Kozak sequence, which is a sequence for effectively translating mRNA in eukaryote (Kozak, 1989) is attached prior to the initiation codon." The Kozak et al. reference cited in the instant specification presents the consensus Kozak sequence. Further, the Kozak sequence is included as part of the sequence of the designed refre1 nucleic acid presented in Figure 9 and SEQ ID NO: 1 of the instant application.

Applicants submit that the Kozak sequence (ACCATGG) is well known in the art. In fact, this sequence is readily identified in a Google Search by searching for "Kozak sequence."

In view of the teachings of the instant specification and further in view of the knowledge available to one of skill in the art regarding the consensus Kozak sequence Applicants submit that it is not necessary to refer to this sequence by a sequence identification number. Indeed, the claims are abundantly clear and definite as recited.

In view of all of the above, Applicants respectfully request reconsideration and withdrawal of the rejections.

### ***Claim Rejections***

#### **Rejection of Claims 1-16 under 35 U.S.C. §112, second paragraph**

Claims 1-16 are rejected under 35 U.S.C. §112, 2<sup>nd</sup> paragraph, for alleged indefiniteness.

Claims 3, 6 and 7 have been cancelled.

Additionally, without acquiescing to the grounds for rejection, Applicants have amended the noted claims as follows to clarify the features of the invention.

The Examiner rejected claims 1-2, 7 and 9-12 as "being indefinite in the recitation of the term "gene." Applicants acknowledge that the Examiner has suggested that "gene" be amended to "coding sequence." For clarity, Applicants have amended the claims to replace the term gene with the term "nucleic acid encoding a protein."

The Examiner rejected claim 1 and dependent claims thereof for allegedly being indefinite for omitting essential steps. Applicants have amended claim 1 to clarify the features of the invention.

The Examiner rejected claims 1, 5 and 15 for recitation of the phrase "gene of another species." Applicants have amended the claims to delete the phrase "gene of another species."

The Examiner rejected claims 1, 3, 4 and 5 for recitation of the phrase "region of a factor." Claim 3 is cancelled. Applicants have amended claims 1, 4 and 5 to delete the phrase "region of a factor."

The Examiner rejected claim 1 for recitation of the term "substantially." Applicants have amended claim 1 to delete the term "substantially."

The Examiner rejected claim 2 for recitation of the term "derived." Claim 2 has been amended to recite "the method according to claim 1, wherein the heterologous nucleic acid is derived from yeast."

A definition for the term "derived" is not provided in the specification. Therefore, this term should be given its plain, ordinary and accustomed meaning as understood to one of ordinary skill in the art in view of the specification. "Derived" is defined by Webster's Ninth New Collegiate Dictionary as "to obtain from a specified source."

The Examiner has rejected claim 16 for the recitation "plant is seed". Claim 16 has been amended to recite "a seed produced by the plant according to claim 15."

In view of all of the above, Applicants respectfully request reconsideration and withdrawal of the rejections.

Rejection of Claims 1-16 under 35 U.S.C. §112, first paragraph

Claims 1-16 are rejected under 35 U.S.C. §112, 1<sup>st</sup> paragraph, for allegedly lacking enablement and failing to meet the written description requirement.

For the sake of brevity, these rejections are summarized below and addressed in combination.

#### Enablement

The Examiner states at page 10 of the Office Action that although the specification is "enabling for modified yeast FRE1 coding sequence as defined in SEQ ID NO:1, a transgenic plant and a method of producing said transgenic plant comprising introducing and expressing said coding sequence in said transgenic plant, does not reasonably provide enablement for the scope of possible gene sequences from any species claimed for use in plants."

At page 12 of the Office Action the Examiner states that "[t]he claims encompass any possible nucleic acid gene sequences having any such modifications of a downstream area of a GT-region by replacing any 'region of a factor relating to the poly(A) addition of the mRNA.'"

At page 13 of the Office Action the Examiner states that "[t]he specific modifications to the yeast FRE1 gene taught in the specification and claimed as instant SEQ ID NO: 1 do not provide a substantial correlation to any modification needed or required in any other nucleic acid sequence broadly claimed."

#### Written Description

The Examiner states at pages 18-19 of the Office Action that "[t]he specification does not have adequate written description for genus of nucleic acid sequences comprising a coding sequence which has been modified to encode a functionally unaltered protein... The specific modifications to the yeast FRE1 gene taught in the specification and claimed as instant SEQ ID NO: 1 do not provide a substantial correlation to any such modification needed or required in other nucleic acid sequence broadly claimed."

The rejections are traversed. In view of the teachings of the specification and the knowledge available to one of skill in the art the instant claims are clearly enabled.

Further, in view of the teachings of the instant specification the claims clearly meet the written description requirement.

The claims have been amended to recite specific polyadenylation signal sequences. Amended claim 1 recites "wherein the polyadenylation signal sequence is selected from the group consisting of ATTTA, NATAAA, ANTAAA, AANAAA, AATNAA, AATANA and AATAAN of which N is A, G, C or T." The claims have also been amended to recite "the GT rich sequence is 8 or more consecutive G and/or T nucleotides." In view of the amendments to claim 1, one skilled in the art could easily identify the polyadenylation signal sequences and the GT rich sequences encompassed by the claims, for example by using a computer program or by manual analysis of a sequence.

Further, the instant claims require that the modification(s) of these sequences do not alter the amino acid sequence of the protein encoded by the heterologous nucleic acid. For Example, ATTTA could be modified to ATCTA or other sequences provided that the modification does not alter the amino acid sequence of the protein encoded by the heterologous nucleic acid. In view of the teachings of the specification and the vast amount of knowledge of codon degeneracy available to one of skill in the art, the claimed modified nucleic acid sequences could be constructed readily without undue experimentation.

Furthermore, the present invention is based on the finding that "in the presence of GT-rich base sequence, addition of poly (A) is determined in plants, subsequently mRNA is split at the position after 10-30 bp from the poly (A) signal, for example AATAAA like base sequence, then poly (A) is added by an action of poly (A) polymerase" (see page 8, lines 11-15 of the present application).

Since the transcription of an mRNA from a heterologous nucleic acid and the addition of poly (A) proceed with RNA polymerase and other enzymes of the plant involved in transcription and poly (A) addition, the transcription and addition of poly (A) proceed independently from what is encoded in the heterologous nucleic acid. The present invention is therefore applicable to any heterologous nucleic acid irrespective of what is encoded in the nucleic acid.

Further, the instant specification clearly and explicitly teaches that the modification of a polyadenylation signal sequence and a GT rich sequence in the FRE1 gene does not interfere with expression of FRE1 in tobacco (see Example 9 entitled "Confirmation of Ferric-chelate Reductase").

In view of all of the above, Applicants submit that the claims clearly meet the legal requirements for both enablement and written description.

Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejection under 35 U.S.C. §102(b)

For the sake of brevity, these rejections are summarized below and addressed in combination.

Claims 1, 3-5, 7-8, 14, 15 and 16 are rejected under 35 U.S.C. §102(b) over Perlak et al. (PNAS, 88:3324-3328, 1991).

Claims 1, 5, 7-8, 13, 15 and 16 are rejected under 35 U.S.C. §102(b) over Nayak et al. (PNAS, 94:2111-2116, 1997).

Perlak

The Examiner states at page 22 of the Office Action that "Perlak et al. disclose a method of making a transgenic plant and seeds derived thereof comprising introducing and expressing a modified coding sequence cryIA(b) gene of *Bacillus thuringiensis* in transgenic tobacco and tomato plants. The transgenic plants exhibited improved insect resistance. The modification did not alter the amino acid sequence of the CryIA(b) protein. The modification of coding sequence for cryIA(b) comprised altering AATAAA and/or ATTTA sequences. Furthermore, the modification increased (increase is encompassed by difference) G and C content throughout the region of gene to be introduced, and modification was based on plant preferred codons without changing the amino acid sequence."

Nayak

The Examiner states at page 23 of the Office Action that "Nayak et al. disclose a method of making a transgenic plant and seeds derived thereof comprising introducing and expressing a modified coding sequence cryIAc gene of *Bacillus thuringiensis* in

transgenic rice (grass) plants. The transgenic plant exhibited improved insect resistance. The modification did not alter the amino acid sequence of the cryIAc protein. The modification of coding sequence for cryIAc comprised altering ATTTA sequences. Furthermore, the modification increased...G and C content throughout the region of gene to be introduced, and modification was based on plant preferred codons without changing the amino acid sequence.”

Applicants submit that for a determination of anticipation to be proper, the prior art reference must disclose each and every limitation of the claim. *Atlas Powder Company et al. v. IRECO, Incorporated et al.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999).

The rejections are traversed. Neither of the cited documents teach or suggest the features of the present invention in any manner to sustain either one of the rejections.

Amended claim 1 requires “modifying...the GT rich sequence without altering the amino acid sequence of the protein encoded by the heterologous nucleic acid.”

Perlak et al. teach modifications of the coding sequence of insect control protein genes. Perlak does not teach or suggest “modifying the GT rich sequence” of the gene, as required by instant claim 1 and dependent claims thereof.

Figure 1 of Perlak et al. presents the DNA sequence of the WT and PM (partially modified) cryIA(b) genes wherein the differences between the genes are within the labeled boxed area (A-I). None of the modifications to the PM gene are modifications of a GT rich sequence, as required by instant claim 1.

Nayak et al. teach reconstruction of the cryIAc gene. Nayak et al. state on page 2112, right column, in the section entitled “Reconstruction of a Truncated cryIAc Gene” that “[t]he coding sequences of the cryIAc gene were reconstructed to remove potential RNA processing sequences and polyadenylation signals, and to optimize for more plant-preferred codon usage. Reconstruction was done essentially on the same line as that of Perlak et al”.

Nayak et al. do not teach or suggest “modifying the GT rich sequence” of the gene, as required by instant claim 1 and dependent claims thereof. Indeed, sequences



of 8 or 9 consecutive G- or T- sequences remain in the reconstructed cryIAc nucleotide sequence shown in Fig. 3 of Nayak et al. (positions 529-537, positions 1759-1767).

In view of all of the above, Applicants respectfully request reconsideration and withdrawal of the rejections.

Rejection of Claim 9 under 35 U.S.C. §103(a)

Claim 9 is rejected under 35 U.S.C. §103(a) over Perlak et al. (PNAS, 88:3324-3328, 1991) in view of Kozak.

Perlak is discussed above in Applicants' response to the rejection under 35 U.S.C. §102(b).

Kozak

The Examiner states at pages 24 through 25 of the Office Action that "Kozak teach that Kozak sequence(s) increases the efficiency of binding of an eukaryotic mRNA to ribosome(s) and thus increasing the efficiency of translation initiation during protein synthesis...[i]t would have been obvious for one of...ordinary skill in the art at the time the claimed invention was made to modify Perlak et al. method for transforming a useful plant by adding a step of inserting Kozak sequence to the 5' end of translation initiation codon 'AUG' in bacterial cryIA(b) gene sequence."

The rejection is traversed. The cited documents, even in combination, fail to teach or suggest the features of the present invention in any manner sufficient to sustain the rejection.

**Even if the references are combined, they do not provide the invention as claimed.**

Applicants submit that even if the Perlak et al. reference is combined with the Kozak et al. reference, the combination of disclosures does not provide the invention recited in claim 9. That is, the recited combination lacks essential elements of the claimed invention.

As discussed above, the Perlak et al. reference does not teach or suggest "modifying the GT rich sequence" of a gene. Applicants submit that the Kozak et al. reference does not cure this deficiency. Kozak et al. presents an analysis of the role of flanking nucleotides in the recognition of the AUG initiator codon by eukaryotic ribosomes (see Abstract).

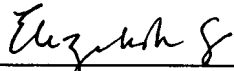
It is well-known that to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference(s) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143.

There is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the cited references to make the claimed invention, nor is there a reasonable expectation of success. Accordingly, reconsideration and withdrawal of the rejection are requested.

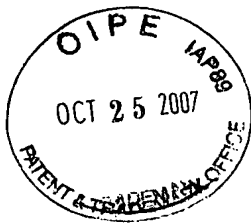
In view of the above amendments and remarks, Applicant believe the pending application is in condition for immediate allowance.

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Respectfully submitted,

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ANNOTATED SHEET

14/19

*FRE1*

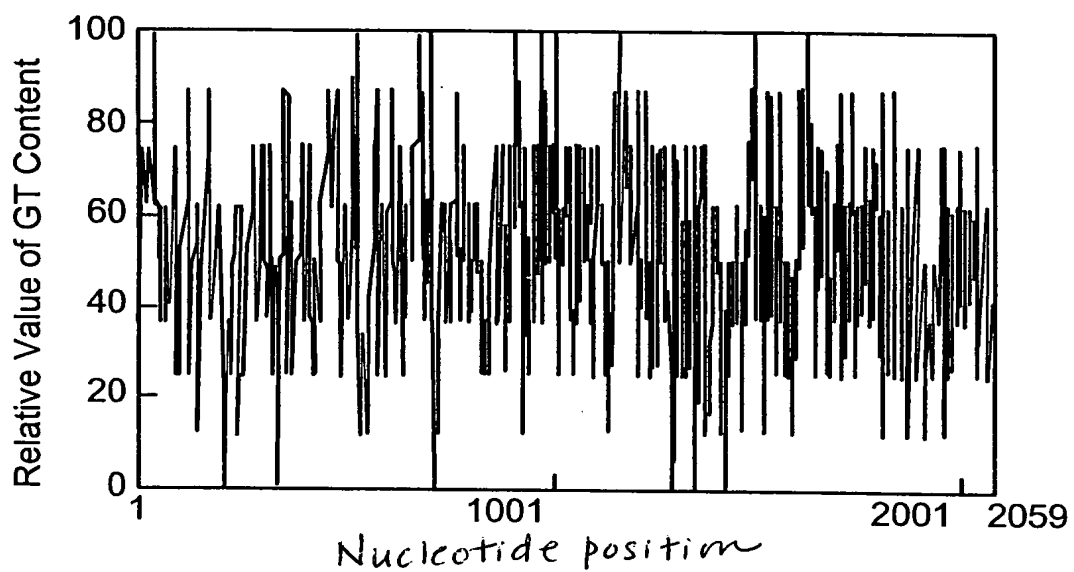


FIG. 10A

*refre1*

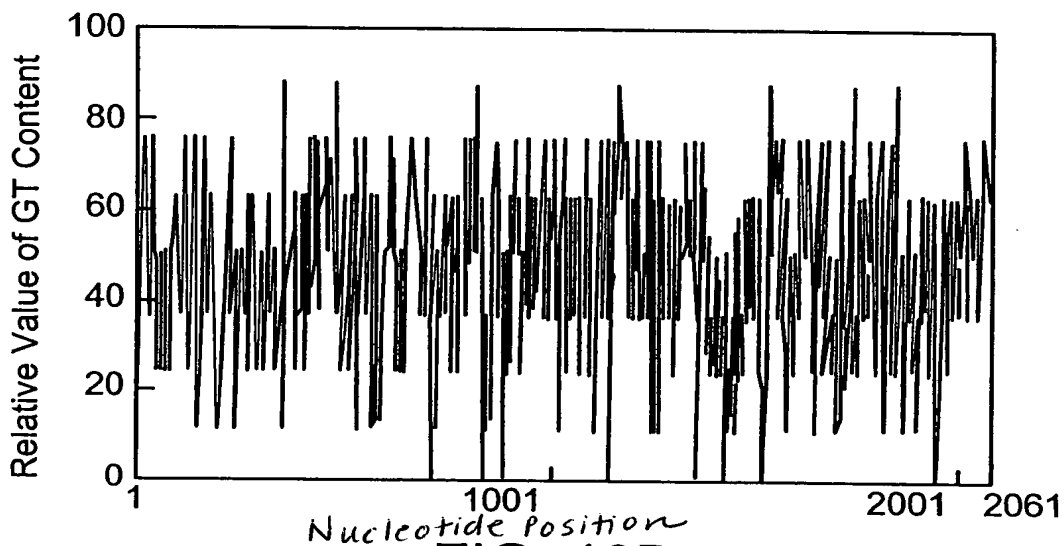


FIG. 10B